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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/252,828	02/19/1999	KE-WEN DONG	024754/0114	4940

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EXAMINER
COOK, LISA V

ART UNIT	PAPER NUMBER
1641	39

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/252,828	DONG ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 March 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Response

1. Applicant's amendment and response filed 18 March 2003 in Paper #38 is acknowledged. In amendment-L filed therein claims 61,62, and 66 were modified. Currently, Claims 48-68 are pending and under consideration.

OBJECTIONS MAINTAINED

Drawings

2. Applicants corrected drawings filed 3/18/03 have been received. The drawings remain objected to by the examiner because they do not properly identify the sequences included in the drawings. Specifically figures 1, 2, and 3. Please identify by the appropriate sequence identification number (SEQ ID NO), in order to comply with the sequence rules. See 37 CFR 1.821 through 1.825 for the Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form 1449 has cited the references they have not been considered.

Applicant stated that an Information Disclosure Statement was filed in response to the examiner request (paper #12,filed 6/28/00), however no record of such IDS is found in the instant application. Applicant is invited to re submit the papers.

NEW GROUNDS OF REJECTIONS

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 50, 52, 61, and 62 are withdrawn rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record in paper #8. Applicants have amended the cited claims therein obviating the rejections below:

A. Claims 50, 52, 61, and 62 are objected to because of the terms "active portion" and "polypeptide portion" are relative terms. The relative terms render the claim indefinite. They are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. As recited it reads on any complex form, which may have been produced by some other means. It is suggested that the actual structures be included in the claims in order to obviate this rejection. (i.e. sequence identification numbers).

Specification

5. The use of the trademarks has been noted in this application. They should be capitalized wherever it appears and be accompanied by the generic terminology. For example see Sephadex on page 17 and Tween on page 22. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 48-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In particular, the claims are drawn to a purified recombinant glycoprotein, wherein the protein has the following properties: (i) of 65kd to 100kd; (ii) comprises approximately 40% to 60% carbohydrate by weight and binds human spermatozoa at least 10 times as strong as an equivalent molar amount of mouse ZP3; (iii) and can stimulate the acrosome reaction of human spermatozoa when co-present with the spermatozoa at a concentration of less than 1μg/ml for a time period less than one hour.

The claims and specification fail to provide the identity or structure of the isolated polypeptide sequences. The specification does not provide evidence of an amino acid sequence meeting the instantly claimed function, other than sequence of SEQ ID NO: 1.

The specification at page 14 the last line recites "Accordingly, a peptide according to one embodiment is more than 46% identical to human ZP3 sequence shown in SEQ ID NO:1"; however the specification does not state the identity by amino acid sequence or any structural characteristics of any other sequence that has the claimed characteristics. Moreover, there is evidence that other sequences have not yet been identified therefore; applicants' vague description of an isolated purified glycopolypeptide comprising sequence identification number 2 has not been adequately described. In view of the lack of evidence, it is apparent that Applicants were not in possession of additional sequences, at the time of filing the instant application.

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed structure of the isolated/purified glycopolypeptide sequence, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention. The structure is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. The protein activity characteristics, weight compositions and binding affinity requirements distinguish the protein only by what it does,.i.e., protein activity, which are purely functional distinctions. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is.

The instant specification and claims describe an isolated/purified glycopolypeptide by function, however this description does not describe the claimed protein itself.

See also, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), where the court held that a generic statement that defines a genus of structures by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA/PROTEIN molecules, usually defined by a nucleotide/amino acid sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". Thus a skilled artisan cannot envision all the contemplated nucleotide/amino acid sequences by the detailed chemical structure of the claimed polynucleotides/polypeptides and therefore conception cannot be achieved until reduction to practice has occurred.

Thus, in the absence of sequence information of the glycopolypeptide of 65kd to 100kd comprises approximately 40% to 60% carbohydrate by weight and binds human spermatozoa at least 10 times as strong as an equivalent molar amount of mouse ZP3; and can stimulate the acrosome reaction of human spermatozoa when co-present with the spermatozoa at a concentration of less than 1μg/ml for a time period less than one hour, a glycopolypeptide described only by its protein activity fails to meet the written description requirements. Therefore only SEQ ID NO:1 and not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

I. Claims 48-56 and 60-68 are rejected under 35 U.S.C. 102(b)(e) as being anticipated by Dean (U.S.Patent#5,641,487).

Dean disclosed a polypeptide and functional derivatives thereof, which have human ZP3 activity or human ZP3 antigenicity. The polypeptides can be produced either synthetically or by recombinant DNA technology. Specifically, the polypeptide to be expressed is coded for by a DNA sequence or more accurately a nucleic acid sequence. The nucleic acid sequence is optionally transcribed and translated to the target polypeptide via cloning into a vector transformed into a host cell. The vector may be self-replicating or it may integrate into the DNA of the host. (see abstract, claims, and columns 1-4). The resulting glycopolypeptides produced in this invention comprised several amino acid lengths and they were found to be 97.1% homologous with the instant invention product in SEQ ID NO:2. (MPSRCH comparing protein-protein database search utilizing BLOSUM62 – GenCore version 4.5).

II. Claims 48-56 and 60-68 are rejected under 35 U.S.C. 102(b)(e) as being anticipated by Dean (U.S.Patent#5,672,488).

Dean disclosed a polypeptide and functional derivatives thereof, which have human ZP3 activity or human ZP3 antigenicity. The polypeptides can be produced either synthetically or by recombinant DNA technology. Specifically, the polypeptide to be expressed is coded for by a DNA sequence or more accurately a nucleic acid sequence. The nucleic acid sequence is optionally transcribed and translated to the target polypeptide via cloning into a vector transformed into a host cell. The vector may be self-replicating or it may integrate into the DNA of the host. (see abstract, claims, and columns 1-4). The resulting glycopolypeptides produced in this invention comprised several amino acid lengths and they were found to be 97.1% homologous with the instant invention product in SEQ ID NO:2. (MPSRCH comparing protein-protein database search utilizing BLOSUM62 – GenCore version 4.5).

Response to Arguments

In response to the argument that the Dean patents only teach a 16 amino acid sequence epitope of residues 327-342 (SEQ ID 11) while SEQ ID No:2 has 41 residues. This argument was carefully considered but not found persuasive because the GenCore version 4.5 indicate that the Dean patents include a 41 residue sequence 97% homologous to Seq Id No:2. Both sequences are 424 amino acids in length, in '487 the comparative sequence is number 4 and in '488 the comparative sequence is number 7 and are amino acid numbers 308-348. Therefore the sequence taught by Dean comprise the instantly claimed sequence. The results are attached.

With respect to functional language, it is noted that whether or not the functional limitation complies with 35 U.S.C. 112, second paragraph is a different issue from whether the limitation is properly supported under 35 U.S.C. 112, first paragraph or is distinguished over the prior art. MPEP 2173.05(g) In response to applicant argument that no prima facie case of obviousness has been established with regard to "a glycopolypeptide that can bind human spermatozoa at least 10 times as strong as an equivalent molar amount of mouse ZP3", it is noted that the cited references disclose sequence identification number 2. The functional language of applicants claim do not render the claim patentable over the prior art.

The functional recitation has not been given patentable weight because it is narrative in form. In order to be given patentable weight, a functional recitation must be expressed as a "means" for performing the specified function, as set forth in 35 USC § 112, 6th paragraph, and must be supported by recitation in the claim of sufficient structure to warrant the presence of the functional language. *In re Fuller*, 1929 C.D. 172; 388 O.G. 279.

Further, it has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

Further see, MPEP 2113 [R-1] Product-by-Process Claims "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 57-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dean (U.S.Patent#5,641,487) or Dean (U.S.Patent#5,672,488) in view of Chamberlin et al. (Proc.Natl.Acad.Sci.USA, Developmental Biology, Vol.87, pp.6014-6018, August 1990) and in further view of Stern et al. (U.S.patent#5,869,053).

Please see previous discussions of Dean(5,641,487) and Dean(5,672,488) as set forth above.

Dean(5,641,487) and Dean(5,672,488) differ from the instant invention in not identifying the specific full-length structure of Human ZP3 cDNA and the specific transducing cell line of the PA-1.

However, Chamberlin et al. disclose this limitation in the reference found in the Proc.Natl.Acad.Sci.USA, Developmental Biology, Vol.87, pp.6014-6018, August 1990. The full-length was previously established in this teaching. Chamberlin et al. take advantage of the cross-hybridization of the mouse cDNA and human DNA to isolate and characterize the full-length cDNA clones of human ZP3 (deposited in the GenBank data base-accession no.M35109). Human ZP3 cDNA was purified from total RNA isolated from a human ovary and used as the first-strand synthesis with oligonucleotide primer A2T15. The first-strand was amplified by PCR.

Further, the utility of the PA-1 (human ovarian carcinoma) cell line in PCR techniques involving glycoproteins was also established. In the patent of Stern et al. the glycoprotein 5T4 was identified in human trophoblast. In table III, the reactivity of MAB 5T4 with normal cells and transformed cell lines in cell-surface immunofluorescence and radiobinding assays showed a comparatively high binding index (4.9 in the Ovary cell PA-1.

A comparison of reactivity with negative control xenogeneic cell lines indicated positive expression of the antigen. (Column 8, lines 52-61) Dean(5,641,487), Dean(5,672,488), Chamberlin et al., and Stern et al. are analogous art because they are from the same field of endeavor, all the cited inventions teach method involving glycoprotein production and isolation techniques.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the ovarian cell line PA-1 and human ZP3 as taught by Chamberlin et al., and Stern et al. in either method of Dean(5,641,487) and Dean(5,672,488) to perform glycoprotein production via the transduction of a human ovarian cell line with a polynucleotide that encodes a polypeptide comprising ZP3 because such methods of evaluation as taught by Chamberlin et al., and Stern et al. is well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such techniques, because both the PA-1 cell line and the full-length human ZP3 sequence were established in the prior art.

The motivation to utilize such compounds can be found in the predictable glycosylation sites of ZP3 and its homology to the mouse analogue, which has strong binding affinity for spermatozoa and induces an acrosome reaction. See Chamberlin et al. page 6015 1st and 2nd column.

Response to Arguments

In response to applicant argument that no prima facie case of obviousness has been established with regard to "a glycopolypeptide that can bind human spermatozoa at least 10 times as strong as an equivalent molar amount of mouse ZP3", it is noted that the cited references disclose sequence identification number 2. The functional language of applicants claim do not render the claim patentable over the prior art.

With respect to functional language, it is noted that whether or not the functional limitation complies with 35 U.S.C. 112, second paragraph is a different issue from whether the limitation is properly supported under 35 U.S.C. 112, first paragraph or is distinguished over the prior art. MPEP 2173.05(g)

The functional recitation has not been given patentable weight because it is narrative in form. In order to be given patentable weight, a functional recitation must be expressed as a "means" for performing the specified function, as set forth in 35 USC § 112, 6th paragraph, and must be supported by recitation in the claim of sufficient structure to warrant the presence of the functional language. *In re Fuller*, 1929 C.D. 172; 388 O.G. 279.

Further, it has been held that the recitation that an element is "capable of" performing a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchison*, 69 USPQ 138.

In response to the argument that the reference of Stern et al. teaches away from the instant invention and is applied in hindsight it is noted arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Stern et al. were merely cited to establish that the PA-1 cell line was previously disclosed in the prior art.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Further see, MPEP 2113 [R-1] Product-by-Process Claims "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

9. For reasons aforementioned, no claims are allowed.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
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5/27/03

LONG V. LE
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